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# How can we improve outcomes of chlamydia control programmes?



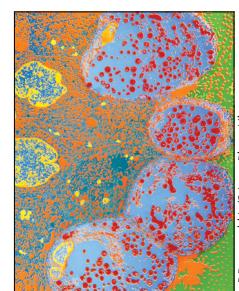
*Chlamydia trachomatis*, the most common sexually transmitted bacterial infection, can have important adverse consequences for women's reproductive health. Chlamydia can cause salpingitis, which can be either symptomatic (pelvic inflammatory disease) or asymptomatic, and its sequelae, ectopic pregnancy and tubal factor infertility.<sup>1</sup> Given highly effective therapy and excellent diagnostic tests, chlamydia control programmes to reduce and prevent adverse reproductive consequences have been initiated widely. In *The Lancet Infectious Diseases*, Bethan Davies and colleagues<sup>2</sup> present a careful evaluation and thoughtful discussion of the risks of reproductive complications in a nationally representative sample of Danish women after being tested (and presumably treated) for chlamydia infection.

The study took advantage of Denmark's comprehensive population register, which could be linked to hospital records for inpatient, outpatient, and emergency room visits and chlamydia test results. The investigators created a retrospective cohort of reproductive aged women (15–44 years old) who tested positive after Jan 1, 1995 (when chlamydia infection reporting was compulsory) and four matched controls who were not tested or had only negative chlamydia tests. This cohort (516 720 women: 103 344 positive, 182 879 negative, and 230 497 never-tested) is the largest group studied so far. Complications were captured until Oct 31, 2012, with mean follow-up of 8 years.

As has been seen elsewhere, women with a positive chlamydia test were at a 30% or greater increased risk of pelvic inflammatory disease.<sup>3,4</sup> There was also increased risk for ectopic pregnancy and tubal factor infertility as compared with women who were chlamydia-negative, but the impact on health was modest; the difference in incidence of complications was small (pelvic inflammatory disease 0.6%; ectopic pregnancy 0.2%; tubal factor infertility 0.1%). Repeat infections increased the risk of pelvic inflammatory disease by a further 20%, again consistent with older studies.<sup>5</sup> By contrast, complication risk was more than 60% lower in never-tested women, suggesting criteria for testing effectively identified those at risk.

The obvious question is why is there excess risk for disease associated with chlamydia infection after diagnosis and treatment? With ectopic pregnancy and tubal factor infertility, the obvious answer is that these reflect previous Fallopian tube damage (scarring), which can occur with or without a previous symptomatic pelvic inflammatory disease episode. But why the excess risk of pelvic inflammatory disease? The intuitive answer is that chlamydia infection is a surrogate for other sexually transmitted infections that cause pelvic inflammatory disease. In Denmark, the incidence of gonorrhoea has been declining for years so gonococcal infection is not a likely candidate.<sup>6</sup> However, *Mycoplasma genitalium* or ascendance of bacteria associated with bacterial vaginosis could be other candidates.<sup>7</sup>

But could the excess pelvic inflammatory disease risk associated with chlamydia infection still be due to chlamydia infection despite its having been diagnosed and treated? This is not a trivial question, and the answer could have important consequences for the design of comprehensive control programmes that go beyond screening. It is likely that answers to some questions are available from further examination of the dataset and were only partly addressed by adjustment for year of testing cohort. For example, what was the treatment rate for women diagnosed with chlamydia infections and for their partners? Were reinfections missed? Knowing the frequency of chlamydia testing for repeat screening of cases could help here. Although annual screening of sexually active adolescent and young adult women is recommended, only in recent years has there been a major emphasis on repeat testing at 3 months after diagnosis to identify reinfection.<sup>8</sup> Longer than recommended testing intervals could miss reinfections as these are likely to be of shorter duration than primary infections. What were the results of diagnostic tests done when pelvic inflammatory disease was diagnosed? Could secular changes in chlamydia test technologies or patient management have affected the size of risk identified in this study? Antigen detection methods used during 1995–2000 could have missed 50% of infections detectable by second-generation nucleic acid amplification



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tests available afterwards.<sup>9,10</sup> Patients with pelvic inflammatory disease were once routinely admitted to hospital and diagnosis of ectopic pregnancy was determined surgically, but both transitioned predominantly to outpatient management.<sup>11</sup> Because ascertainment of complications was based solely on hospital records, further work is needed to see if cohort members attended other primary care settings for milder presentations of complications.

Answers to these questions could help define causes of excess risk of reproductive complications seen after a positive chlamydia test and inform more effective interventions leading to improved outcomes. We look forward to further mining of this valuable dataset.

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We declare no competing interests.

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